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Identifying Airborne Pathogens in Time to Respond

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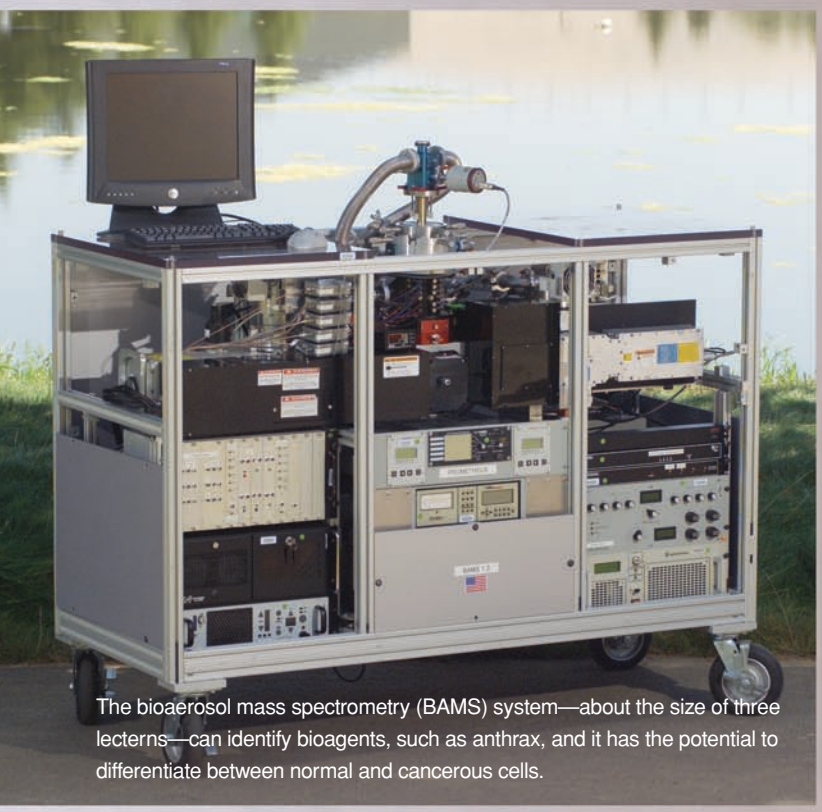
AMONG the possible terrorist activities that might threaten national security is the release of an airborne pathogen such as anthrax. Because the potential damage to human health could be severe, experts consider 1 minute to be an operationally useful time limit for identifying the pathogen and taking action. Many commercial systems can identify airborne pathogenic microbes, but they take days or, at best, hours to produce results. The Department of Homeland Security (DHS) and other U.S. government agencies are interested in finding a faster approach.

To answer this national need, a Livermore team, led by scientist Eric Gard, has developed the bioaerosol mass spectrometry (BAMS) system—the only instrument that can detect and identify spores at low concentrations in less than 1 minute. BAMS can successfully distinguish between two related but different spore species. It can also sort out a single spore from thousands of other particles—biological and nonbiological—with no false positives. (See *S&TR*, September 2003, pp. 21–23.)



The bioaerosol mass spectrometry (BAMS) system—about the size of three lecterns—can identify bioagents, such as anthrax, and it has the potential to differentiate between normal and cancerous cells.

The BAMS team won a 2005 R&D 100 Award for developing the system. Livermore's Laboratory Directed Research and Development (LDRD) Program funded the biomedical aspects of the BAMS project, and the Department of Defense's Technical Support Working Group and Defense Advanced Research Project Agency funded the biodefense efforts.

Developing a detection system that can analyze small samples so quickly has been challenging. Livermore engineer Vincent Riot, who worked on the BAMS project, explains, "A typical spore weighs approximately one-trillionth of a gram and is dispersed in the atmosphere, which contains naturally occurring particles that could be present at concentrations thousands of times higher. Previous systems also had difficulty separating benign organisms from those that are pathogenic but very similar, which has resulted in false alarms."

Sorting between Harmful and Benign

BAMS operates by drawing air through a nozzle and removing nearly all the particles too small to be biological threat agents. The remaining particles—each about 0.5 to 10 micrometers in diameter—are focused into a tight beam. A particle accelerates to a velocity determined by its size and shape, which provides information on a particle's type. The system then probes each particle to determine if it contains biological material. For this operation, a pulsed-laser beam excites the particles. Biological materials, if present, emit fluorescent light, which can be recorded by the detector, but nonbiological particles, such as dirt in the atmosphere, do not emit light. This step reduces the number of particles for further analysis by 90 percent.

In the system's final step, a mass spectrometer identifies the particles. Most mass spectrometers operate by measuring either positive or negative ions. BAMS uses a dual-polarity mass spectrometer, which can process a particle's positive and negative ions at the same time. The positive and negative ions formed are further separated by polarity and mass-to-charge ratio. Real-time pattern-recognition software developed at the Laboratory then analyzes and categorizes the resulting spectra. Every organism produces a unique signature, which BAMS compares with spectra in a database of organisms. The system can analyze thousands of

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particles per second, so it can distinguish a very small concentration of biological aerosol from a much larger concentration of background aerosol.

To test the system, the Livermore team used *Bacillus subtilis var. niger*, a surrogate of anthrax (*B. anthracis*), and *B. thuringiensis*, an organic pesticide that differs from *B. anthracis* in two short sections of its DNA. BAMS successfully distinguished between the two. The instrument also identified other bacterial cells and spores, biological toxins, and viruses. "BAMS is the only system that can identify harmful biological agents in enough time to evacuate an area," says Riot, "and it can do so with almost no false positives, which is essential in reducing the panic that alarms can cause."

In a recent study, the team placed BAMS in the international terminal at San Francisco International Airport to help DHS determine the cause for false positives registered by other equipment. The instrument has also been used in preliminary studies at Livermore's Site 300, where BAMS successfully distinguished particles in the atmosphere and surrounding soil from those generated by a detonation of conventional high explosives.

The system's ability to analyze particles or cells could benefit other fields in addition to biological threat detection. Potential applications include medical diagnostics, explosives detection, meteorological studies, and nonproliferation programs. For example, the BAMS team hopes to build on the Site 300 research to develop detection capabilities for radioisotopes, which would benefit the nation's nonproliferation programs.

Detecting Communicable Airborne Diseases

BAMS also has the potential to detect communicable diseases such as severe acute respiratory syndrome (SARS) or tuberculosis, which typically take about a week for clinical detection. Livermore researchers have used tuberculosis surrogates to test the system's ability in this area. The LDRD Program is funding an effort to analyze human sputum. Led by physicist Matthias Frank, the project includes researchers from the Laboratory's Chemistry and Materials Science; Physics and Advanced Technologies; Nonproliferation, Arms Control, and International Security; and Biosciences directorates. By learning which particles occur naturally, these scientists hope to find a method for detecting abnormal cells for various diseases. Riot says, "The idea is to have a person breathe into a mask, then let BAMS analyze the particles released from the lungs and identify them instantaneously."

Members of the BAMS development team: (left to right, back row) Paul Steele, Todd Weisgraber, Bruce Woods, Abneesh Srivastava, and Keith Coffee; (middle row) Vincent Riot, Jim Birch, Herbert Tobias, and Eric Gard; (front row) Matthias Frank and David Fergenson.

The current BAMS system, about the size of three lecterns, is available for licensing. The Livermore team continues to work on improving the system's capability and reducing its size to fit various needs. Whether used to detect biological agents or contagious diseases, BAMS shows great promise for identifying problems reliably when time is of the essence.

—Gabriele Rennie

Key Words: airborne pathogen, anthrax, bioaerosol mass spectrometry (BAMS) system, R&D 100 Award.

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